

Amendment dated July 31, 2009

Reply to Notice to Comply mailed July 1, 2009

Amendments to the Specification:

Please replace the paragraph being on page 3, line 21 with the following amended paragraph:

In a first aspect, the present invention provides a method of increasing muscle function in a subject, said method comprising administering to said subject an agent selected from the group consisting of (a) a growth hormone (GH) secretagogue and (b) a composition comprising a GH secretagogue and a pharmaceutically acceptable carrier. In an embodiment, the GH secretagogue is selected from the group consisting of GH-releasing factor (GRF) and a GRF analog. In another embodiment, the GRF analog is a GRF analog of formula A:

X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B) (SEQ ID NO: 1)

wherein,

A1 is Tyr or His;

A2 is Val or Ala;

A8 is Asn or Ser;

A13 is Val or Ile;

A15 is Ala or Gly;

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A18 is Ser or Tyr;

A24 is Gln or His;

A25 is Asp or Glu;

A27 is Met, Ile or Nle

A28 is Ser or Asn;

A30 is a bond or amino acid sequence of 1 up to 15 residues; and

R0 is NH₂ or NH-(CH₂)_n-CONH₂, with n=1 to 12; and

X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

wherein the backbone can be substituted by C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or C₆₋₁₂ aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated C₃₋₉ cycloalkyl, and C₆₋₁₂ aryl.

Please replace the paragraph being on page 8, line 32 with the following amended paragraph:

In another aspect, the present invention provides use of an agent selected from the group consisting of (a) a growth hormone (GH) secretagogue and (b) a composition comprising a GH secretagogue and a pharmaceutically acceptable carrier; for increasing muscle function in a subject. In an embodiment, the GH secretagogue is selected from the group consisting of GH-releasing factor (GRF) and a GRF analog. In another embodiment, the GRF analog is a GRF analog of formula A:

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X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B) (SEQ ID NO: 1)

wherein,

A1 is Tyr or His;

A2 is Val or Ala;

A8 is Asn or Ser;

A13 is Val or Ile;

A15 is Ala or Gly;

A18 is Ser or Tyr;

A24 is Gln or His;

A25 is Asp or Glu;

A27 is Met, Ile or Nle

A28 is Ser or Asn;

A30 is a bond or amino acid sequence of 1 up to 15 residues; and

R0 is NH₂ or NH-(CH₂)_n-CONH₂, with n=1 to 12; and

X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

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wherein the backbone can be substituted by C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or C₆₋₁₂ aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated C₃₋₉ cycloalkyl, and C₆₋₁₂ aryl.

Please replace the paragraph being on page 14, line 23 with the following amended paragraph:

In a further aspect, the present invention provides a package comprising (i) an agent selected from the group consisting of (a) a growth hormone (GH) secretagogue and (b) a composition comprising a GH secretagogue and a pharmaceutically acceptable carrier; and (ii) instructions for increasing muscle function in a subject. In an embodiment, the GH secretagogue is selected from the group consisting of GH-releasing factor (GRF) and a GRF analog. In another embodiment, the GRF analog is a GRF analog of formula A:

X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B) (SEQ ID NO: 1)

wherein,

A1 is Tyr or His;

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A2 is Val or Ala;

A8 is Asn or Ser;

-A13 is Val or Ile;

A15 is Ala or Gly;

A18 is Ser or Tyr;

A24 is Gln or His;

A25 is Asp or Glu;

A27 is Met, Ile or Nle

A28 is Ser or Asn;

A30 is a bond or amino acid sequence of I up to 15 residues; and

R0 is NH₂ or NH- (CH₂) n-CONH₂, with n=l to 12; and

X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

wherein the backbone can be substituted by C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or C₆₋₁₂ aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated C₃₋₉ cycloalkyl, and C₆₋₁₂ aryl.

Please replace the paragraph being on page 20, line 1 with the following amended paragraph:

In yet a further aspect, the present invention provides a composition for increasing muscle function in a subject, the composition comprising (a) a growth hormone (GH) secretagogue and (b) a pharmaceutically acceptable carrier. In an embodiment, the GH

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secretagogue is selected from the group consisting of a GH-releasing factor (GRF) and a GRF analog. In a further embodiment, the GRF analog is a GRF analog of formula A:

X-GRF Peptide (A)

wherein;

the GRF peptide is a peptide of formula B;

A1-A2-Asp-Ala-Ile-Phe-Thr-A8-Ser-Tyr-Arg-Lys-A13-Leu-A15-Gln-Leu-A18-Ala-Arg-Lys-Leu-Leu-A24-A25-Ile-A27-A28-Arg-A30-R0 (B).(SEQ ID NO: 1)

wherein,

A1 is Tyr or His;

A2 is Val or Ala;

A8 is Asn or Ser;

A13 is Val or Ile;

A15 is Ala or Gly;

A18 is Ser or Tyr;

A24 is Gln or His;

A25 is Asp or Glu;

A27 is Met, Ile or Nle

A28 is Ser or Asn;

A30 is a bond or amino acid sequence of 1 up to 15 residues; and

R0 is NH₂ or NH-(CH₂)_n-CONH₂, with n=1 to 12; and

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X is a hydrophobic tail anchored via an amide bond to the N-terminus of the peptide and the hydrophobic tail defining a backbone of 5 to 7 atoms;

wherein the backbone can be substituted by C₁₋₆ alkyl, C₃₋₆ cycloalkyl, or C₆₋₁₂ aryl and the backbone comprises at least one rigidifying moiety connected to at least two atoms of the backbone;

said moiety selected from the group consisting of double bond, triple bond, saturated or unsaturated cycloalkyl, and C₆₋₁₂ aryl.

Please replace the sequence listing with the substitute sequence listing filed herewith and insert the substitute sequence listing into the application following the Abstract.